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SENT VIA E-MAIL (sdupont@pmprb-cepmb.gc.ca)

October 6, 2008

Ms. Sylvie Dupont
Secretary to the Board of PMPRB
Box L40
Standard Life Centre
333 Laurier Avenue West Suite 1400
Ottawa, Ontario, K1P 1C1

Dear Ms. Dupont

The purpose of this document is to highlight Merck Frosst's support of Canada's Research-Based Pharmaceutical Companies (Rx&D) submission to the PMPRB Board re: the PMPRB Board's Notice & Comment on Proposed Revisions to the Excessive Price Guidelines released on August 20, 2008 (copy attached). We would also like to reiterate certain concerns expressed in the Rx&D response.

Merck Frosst, through participation in Rx&D activities, has been actively engaged in the consultation around the PMPRB Proposed Guideline Changes. It appears, as reflected in the document, that the proposals identified have not taken into account some key recommendations, discussions and submissions by either Rx&D or the stakeholder working groups. As a result, the proposed revisions to the Guidelines are complex, many aspects lack clarity and detail, and key provisions of the March 2008 Compendium have been omitted. We have concerns that the day to day operations of the biopharmaceutical industry and the intricacies of its market have not been taken into account.

For example, the proposal does not address the complex interrelatedness of the three key issues of the January 2008 Discussion Paper: Any Market Review, Full Reporting of Benefits and the changes to the Consumer Price Index (CPI) Methodology. The pharmaceutical market has become more competitive than ever with provinces demanding benefits, which under the current proposal will cause the Average Transaction Price (ATP) to fluctuate, causing the current CPI-Methodology to be impractical moving forward.

The PMPRB proposed model to de-link the Maximum Non-Excessive Price (MNE) with the Average Transaction Price (ATP) is not de-linking as the MNE will fluctuate with the ATP. Market forces, including review of drugs by the Common Drug Review and provincial committees, and the reimbursement decisions by public and private plans, ensure that prices are cost-effective and fall below the MNE threshold.

The problem of trying to solve these interrelated issues is the paradox inherent with the current CPI-Adjustment Methodology, which bases the MNE on a previous net ATP. Therefore, an ATP considered non-excessive in one year can be considered excessive in future years. For example, if product A is sold in Canada at an average price $1 in 2000 and is within PMPRB guidelines, an ATP of $1 in 2008 should not be considered excessive, regardless of how the ATP progressed between the time periods.

Hence, instead of being rewarded for offering benefits to customers, patentees are actually penalized. Consequently, although the Board states that, "it does not wish to unduly create a disincentive to the offering of the benefits to customers", both its current and proposed Guidelines changes clearly create a disincentive for patentees to offer benefits to customers. This paradox of having a mandate that ensures prices are not-excessive yet at the same time penalizing patentees for offering benefits to customers can only be addressed through a "true-delinking model." Consequently, this is the essence of where the current proposal falls short.

True de-linking of the ATP from the MNE would involve an adjustment in the CPI-Adjustment Methodology, whereby MNE prices in subsequent years would be based on the MNE price in the introductory year, adjusted for changes in the Consumer Price Index, rather than the net ATP, as is currently the situation today. This approach is definitely consistent with the Patent Act and could be used as a basis for establishing a model that is much simpler and less cumbersome for both the Board and the patentee.

In practice, this solution will enhance competition since there is presently no incentive to offer significant discounts. It would also remove the incentive to charge the highest possible price during the introductory period. Since it sets the maximum price for a particular medicine in a specific dosage form and strength, it can be published. This way, this option would provide patentees the flexibility they need to compete while ensuring consumers **never** pay excessive prices.

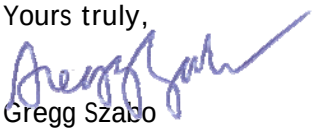
Unfortunately, without a true de-linking model, the PMPRB proposal will produce serious unintended consequences. Patentees in certain markets and certain periods of a product lifecycle could be discouraged from offering benefits to customer. Patentees may be encouraged to discontinue compassionate use programs or not to launch strengths of medicines intended for targeted populations of patient groups in need of important medicines. The uncertain pricing environment impacts business planning and makes it more difficult for Merck Frosst, a subsidiary of Merck & Co., to compete globally for new investments.

Moreover, reviewing prices in 17 proposed markets rather than one will clearly increase the workload for both PMPRB and patentees, who will need to ensure compliance in 17 markets rather than only one market. The proposals would create an additional regulatory burden for patentees that contradicts the policy objectives set out in the federal *Cabinet Directive on Streamlining Regulation* issued on April 1, 2007.

In closing, Merck Frosst endorses the recommendations of Rx&D in their submission document. We reiterate that the critical issue to be resolved is the CPI methodology paradox through a true delinking model. Merck Frosst encourages a partnership approach that is educational, and focuses on reaching a consensus on a viable solution that provide wins for not only all stakeholders but most importantly patients. A patient-centered approach with access to medicines should be the center of creating regulatory changes.

The attached appendix sets out some specific issues and concerns to illustrate the difficulties with the proposed revisions to the Guidelines. We also include our solutions to the issues and concerns. Due to the complexity of the proposed revisions, we hope to be able to make further submissions.

Yours truly,



Gregg Szabo
Executive Director, Policy, Reimbursement & Communications

Appendix: Merck Frosst Technical Submission to PMPRB

This appendix addresses the issues and concerns of Merck Frosst resulting from the PMPRB's Notice and Comment on Proposed Revisions to the Excessive Price Guidelines published August 20, 2008. Due to the complexity of the proposed revisions, we hope to be able to make further submissions.

1. Issue - Underlying Principles

We support Rx&D's recommendation that g*iven the potential for misinterpretation of the Board's mandate, we recommend that the Board not include "… thereby protecting consumers and contributing to Canadian healthcare" in its mandate statement in the Compendium."*

2. Issue - Levels of Therapeutic Improvement

Merck Frosst supports Rx&D's recommendation *that the Board reconsider the need for assessing therapeutic improvement as part of a package of examining ways to simplify its Guidelines proposals and approach to fulfilling its mandate.* Until it does so, we also support the recommendation of *proceeding with the proposal to establish a "moderate improvement" category for price review purposes provided that the price test provides greater flexibility than currently exists for such drugs.*

3. Issue - International Therapeutic Class Comparison (ITCC) Test

Merck Frosst agrees with PMPRB's proposal that the ITCC will not normally be used as a price test for a new patented medicine but should be used to the extent that it may aid in resolving a dispute with a patentee prior to the referral to the Board for a hearing. It is our understanding that this is consistent with the PMPRB's informal practice in the past.

Merck Frosst also agrees with Rx&D's recommendation that *the Board should amend the proposed Schedule 7 to exclude generic drugs from the ITCC.*

4. Issue - Introductory Price Tests

We are very concerned by the absence of several key provisions of the current Guidelines in the proposed draft Guidelines, most notably, provisions governing the Reasonable Relationship (RR) test and the Therapeutic Class Comparison (TCC) test. It is troubling that a rationale is not provided in the Notice and Comment document for their omission.

Although the text of the Notice and Comment states that "It is also agreed to maintain the RR test for line extensions where no therapeutic improvement is proposed," the draft Guidelines includes significant changes which were not the subject of consultation or prior notice:

Test 3: Different Strength Test
On page 29 of the Compendium of Guidelines, Polices and procedures, March 2008, it states that:

> *"If the new DIN is of a lower strength (relative to the critical comparable DIN), the maximum non excessive price for the new DIN is the price/unit of the critical comparable DIN."*

This provision for a new DIN of a lower strength has been omitted in the new proposal. They provide that the MNE of the new DIN be determined on a price/kg basis. In the Pharmaceutical Industry, prices are not set on a price/kg basis. Lower strengths are often developed and formulated to meet

the needs of specific populations unable to tolerate the "standard" dose. Notably both doses are therapeutically equivalent for the respective populations and require the same resources to research and develop. There would be a disincentive to launch products for specific populations if the ability to flat price was abolished

Merck Frosst agrees with the Rx&D recommendation that *this provision should be reinstated.*

8.3 – Category 1 New Drug Products
On page 11 of the Compendium of Guidelines, Polices and procedures, March 2008), it states that:

> *When the above methodology is not considered adequate or appropriate, Board Staff may conduct a Therapeutic Class Comparison Test (Schedule 2) to determine if the introductory price of the new DIN is excessive. This could be relevant if, for example, the new DIN has a therapeutic use or dosage regimen that differs materially from the other DINs of the same or comparable dosage forms of the medicine.*

The draft Guidelines have deleted this existing provision that provides an alternative when the reasonable relationship test is not appropriate. Merck Frosst agrees with the Rx&D recommendation that this *provision should be reinstated.*

8.6 – Category 3 New Drug Products
On page 12 of the Compendium of Guidelines, Polices and procedures, March 2008), it states that:

> *When it is inappropriate or impossible to conduct a Therapeutic Class Comparison Test, Board Staff will give primary weight to the median of the international prices identified in an International Price Comparison Test (Schedule 3) to determine if the introductory price of the new DIN is excessive.*

The draft Guidelines have omitted a key provision that provides an alternative when the Therapeutic Class Comparison Test is not appropriate. Merck Frosst agrees with the Rx&D recommendation that this *provision should be reinstated.*

Schedule 4 – Measuring the Price in a TCC
(Page 26 of the proposed Compendium of Guidelines, Polices and procedures, August 2008)

Merck Frosst agrees with Rx&D that *Schedule 4, "Measuring the Price", the third paragraph should be amended to read: "For comparison purposes, Board Staff will use the highest publicly available prices for the comparable products" rather than " an appropriate public source for the prices of comparable products" to be determined on a case-by-case basis.*

Schedule 4 lacks both certainty and fairness when using an MNE based on the net ATP. A new product could receive a higher or lower price depending on whether on not the comparator product has rebounded from a "dip". It appears that it would become a question of "chance" in determining a price of a new product, which makes this process unfair and unpredictable. Two new products in the same category could end up with two very different introductory prices depending on the timing of its launch. Comparator prices must be transparent and similar for all patentees, regardless of who owns the patent. Merck Frosst recommends that Board Staff uses the highest publicly available prices for the comparable products.

5. Issue - Modified Guidelines for Certain Patented Generic Drug Products

Merck Frosst is questioning why the pharmaceutical industry was not given an opportunity to provide comment or input. Merck Frosst is surprised that the Board is not applying its own "golden rule" on international price comparisons in the case of patented generic drugs given that Canadian prices of generic drugs have tended to be higher than prices in other countries.

6. Issue: Impact of Reporting Benefits (De-linking of the ATP from the MNE Price)

Merck Frosst supports the Rx&D recommendation that *there is an urgency to address the de-linking issue as quickly as possible, and its proposal for the board to establish a small committee with Rx&D to identify some interim measures pending a more thorough review.*

The Notice and Comment document was released on August 20, 2008. On September 9, 2008, 20 days later, the PMPRB released an excel document with examples of the "delinking methodology" and "any market review". The text in the Notice and Comment is unclear and incomplete, further adding to the complexity of the issues. The examples released on September 9, 2008 to explain the new proposed CPI-methodology do not reflect the actual pricing and reimbursement environment.

Variations exist in benefits. Benefits are provided to some but not all customers in a particular class and over different periods of time not during a particular calendar pricing period. Some benefits get renewed over multi-year contracts. Some may involve volume purchasing or bundles with other products and services. Benefits may be offered directly or provided via group purchasing organizations with different purchasing patterns. To add to the complexity, some benefits are paid in years in which the benefit was not provided.

The primary concern is that the standard proposed for de-linking is overly limiting which adds to our concerns. As written in the text of the proposal:

"In cases where the ATP of a drug product declines from a previous year due to the provision of a benefit(s), as proven by evidence provided by the patentee, once the benefit ends if the patentee provides evidence that the price increase was solely due to the termination of the benefit, the MNE price of the drug product will be the previous highest non-excessive ATP."

It is unclear how a scenario in which a patentee provides multiple benefits to customers over different time horizons would be addressed. There is no explanation to how a benefit will be accounted for if it is not terminated. For example, for a reasonable relationship test or a therapeutic class comparison test how will the Board determine the "higher ATP" when not all benefits are terminated? What if there is disagreement? What is the resolution process? This is very unclear and very concerning, as a patentee could be forced to price newly launched products below the actual ATP without benefits.

Another major concern is the ability to take allowable price increases. This is illustrated in the PMPRB example #1 on De-linking. The pharmacy class uses the "dip" but is only allowed to "rebound" to its original ATP without CPI. T**he appropriate adjustment needs to be to the previous highest non-excessive ATP in any class of customer adjusted for changes in CPI over the relevant time period.** Otherwise**,** this could force a company to unfairly price lower in one customer class over another. Furthermore, a patentee could potentially be punished versus a competitor just for providing benefits. For example, two companies launch competing products in the same class at the same price. Company A sells product A for $10 but provides benefits that drop its ATP to $8 over a three year period. Company B sells product B but provides no benefits but take annual CPI increases of 2%. At the end of three years, Company A, no longer provides a benefit and is forced to sell its product at $10, while

company B could sell its product for $10.61. This is another unintended consequence that true de-linking would avoid.

The "gap" was proposed by the WG-PT as part of the de-linking model to recognize the difference between the MNE price and ATP at launch and to reduce the disincentives to offer benefits because of the CPI methodology. By keeping the introductory MNE constant, and adjusted for changes in the Consumer Price Index, rather than the net ATP, represents a compromise to allow some pricing flexibility while not allowing a price that exceeds the MNE price established by the Board. The WG-PT proposed a method to address the Board's apprehension about the potential for large one-year price increases under the "gap" methodology: to limit a single year increase to 33% of the price gap provided it does not exceed 10% or 15% of the ATP. Under these scenarios, it would potentially take between three and ten years before a price could reach the level that the Board's Guidelines determine to be the maximum non-excessive price. In our view, the "gap" methodology provides a good basis to a viable solution.

We are concerned that the Board has not addressed the issue within the proposal as it was an important element to the overall package.

Finally, examples 1-3, shown below, are some of the illustrations we used during our discussions with the Board staff to demonstrate the potential issues and concerns raised by the new proposals:

Example 1: Benefits included at introduction

	National MNE	**National ATP**	
Year 1 (intro)	$10	$5	Benefit
Year 2	$5 (Previous highest non-excessive ATP)		Benefit Ends

- The benchmark price of a DIN is determined in the introductory period. The current guidelines allows for a patentee's introductory ATP to be at a price up to the product's introductory MNE. According to the text of the proposed guidelines, patentees choosing to offer benefits in the introductory period would be subject to a lower benchmark price.
- The PMPRB examples show that this could resolved by "re-setting" the lowered average price at the level of the highest non-excessive ATP by class of customer. They are not clear however, of what the benchmark price would be if there were multiple benefits, not all terminated, extending across all classes and over multiple periods of time? Consequently, at what benchmark price would patentees be permitted to take price increase?
- Depending on the situation, drugs would need to be introduced at the full introductory MNE price and/or offer benefits after the introductory period. **This has serious implications for compassionate use programs.**
- The proposed solution has potential to become very cumbersome and increase workload for both PBPRB and patentees
- The proposed solution does not account for the national MNE potentially being lowered
- **A true delinking model would solve this dilemma**

Example 2: Current Proposal does not allow for Price Increases

Year	**National MNE**	**National ATP**	**Province A**	**Province C**

			ATP	**ATP**
Year 1	$10	$10	$10	$10
Year 2	$10 + CPI	$7.65	$10.30 (+ 3% CPI)	$5 (benefit)
Year 3	**$7.65 + CPI**	$7.65	$10.30 (excessive?)	$5 (benefit)
Year 4	$10 (Previous highest non-excessive ATP)	$10.15 (excessive?)	$10.30 (excessive?)	$10 (benefit ends)

- ❑ This example demonstrates how implementing a price increase in Province A would lead that province to be excessive although it only took allowable CPI increases.
- ❑ A fundamental flaw of the current definition for de-linking methodology as presented in the Draft Guidelines and in the September 9, 2008 examples provided by the PMPRB is that once a benefit expires, the "rebound" is only to the previous highest ATP without CPI considerations.
- ❑ This results in an interpretation that the price is frozen at point *prior to offering benefits* with no allowance for price increases in other markets until the benefit ends
- ❑ Unclear how the Board will interpret benefits that are not terminated
- ❑ Potential to become very cumbersome and increase workload for both PBPRB and patentees
- ❑ **A true delinking model would solve this dilemma**

Example 3: Any Market dilemma

Year	**National MNE**	**National ATP**	**Province A ATP**	**Province B ATP**
Year 1	$10	$10	$10	$10
Year 2	$10 + CPI	$7.50	$10	$5 (benefit)
Year 3	**$7.50 + CPI**	$7.50	$10 (excessive?)	$5 (benefit)
Year 4	$10 (Previous highest non-excessive ATP)	$10	$10	$10 (benefit ends)

- ❑ The text of the draft Guidelines does not clearly present the impact of the de-linking methodology in combination with any market.
  - o The flaw of current definition for de-linking methodology as presented in the draft Guidelines could result in a provincial (or customer) ATP appearing to be excessive on an any-market level even without price increases
  - o September 9, 2008 examples provided by the PMPRB only provide simple examples of how this can be resolved, but does not provide examples with multiple benefits, across different time horizons, which may or may not be terminated.
- ❑ Unclear how the Board will interpret benefits that are not terminated
- ❑ Potential to become very cumbersome and increase workload for both PBPRB and patentees
- ❑ **A true delinking model would solve this dilemma**

7. Issue - Any Market Price Reviews

Merck Frosst agrees with the Rx&D recommendation that the any market issue *requires further work and analysis. The Board should clarify the problem it is seeking to address through any market review, determine the extent of the problem and assess potential solutions accordingly. The Board should be more precise about what it is proposing and the intended impact. In the event the Board*

applies "any market" review and finds a price is excessive, it should base the calculation of excess revenues on the national average transaction price.

Any market price review would apply whenever the National ATP appears to exceed the National MNE. In the case of "de-linking," the examples provided by Board Staff indicate an intention to use any market review when applying the de-linking methodology. It is obvious that if the national ATP dips because of benefits provided, the MNE will consequently decline due to the CPI methodology. Patentees will be excessive in some markets although they never raised their prices. Similarly, there is always risk of the ATP unintentionally rising slightly above the MNE even if there is no change in price; i.e. in the case of a sales mix shift.

The evidence presented in the May 2006 Discussion guide showed that prices for all drugs by class of customer, and by province and territory, were overwhelmingly within the range of 5% of the national MNE price or lower. Under the proposed guidelines patentees will need to monitor their compliance in all 17 submarkets on an ongoing basis in order to avoid the risk of enforcement action by the Board. There is no evidence to suggest that these provisions are necessary as they could result in unsubstantiated claims of excessive pricing.

8. Issue - Re-setting the MNE Price

Merck Frosst agrees with the Rx&D recommendation that *the existing provisions on re-setting the MNE prices of drugs sold under SAP should be reinstated in the Guidelines and they should be applied on a regular basis by Board Staff.*

9. Issue – Unusual Circumstances

Merck Frosst agrees with the Rx&D recommendation *that the Board to work with the Board to develop a more appropriate approach in today's environment to deal with these unusual circumstances that may require patentees to lower prices.*

10. Conclusion:

Merck Frosst realizes that the Notice and Comment package deals with several complex and interrelated issues. We are concerned that these proposed changes could have unintended consequences on the pharmaceutical industry as well as stakeholders in general, especially patients. Merck Frosst remains optimistic that a solution can be reached to ensure an alignment between the objectives of the pricing provisions of the *Patent Act* and the PMPRB mandate and the objectives of the biopharmaceutical industry to ensure Canadian have access to innovative medicines.